

REMARKS

The following remarks are supplemental.

The Rejections Under 35 C.F.R. §§ 102(a) and 103(a)

Claims 1-7 are rejected under 35 U.S.C. § 102(a), as allegedly anticipated by or, in the alternative, under 35 U.S.C. § 103(a), as allegedly obvious over each of four documents, i.e.,

- (1) WO 99/60151 to Kranjc et al. (corresponding to U.S. Patent No. 6,365,382);
- (2) U.S. Patent No. 6,043,064 to Davis et al. (corresponding to Japanese Application No. 7-184670 acknowledged at page 2 of the present application);
- (3) U.S. Patent 5,942,423 to Demain et al.; and
- (4) Okazaki et al., J. Antibiot. 36: 1176-1183, 1983.

The Examiner is maintaining these rejections because although the Examiner considered the arguments in the Amendment filed February 9, 2004 that there are differences between microorganisms of the art (ATCC 19795, ATCC 35024, *Actinomadura*, *Nocardia autotrophica*) and the claimed microorganism *Rhodococcus rhodochrous* ATCC 21430, the Examiner asserts that (1) the pending claims are not directed only to *Rhodococcus rhodochrous* ATCC 21430 so that the claims are not specific as to the strains used, and (2) the differences between this strain and microorganisms having no ability to sporulate and showing no hyphal growth in a culture broth cannot be easily assessed.

In response to this rejection, Applicants respectfully point out that Kranjc merely discloses the strain *Amycolatopsis orientalis* ATCC 19795, which is disclosed in Kranjc to be the producer of the antibiotic vancomycin. The document does not disclose or provide any guidance to teach or suggest producing the compounds of the present invention using a microorganism selected from the group of those belonging to the genus *Mycobacterium*, *Corynebacterium*,

Brevibacterium, Rhodococcus, Gordonia, Arthrobacter, Micrococcus, Cellulomonas and Sphingomonas. Furthermore, even if these microorganisms and *Amycolatopsis orientalis* are reclassified as *Nocardia*, as asserted by the Examiner, they are not the same, and Kranjc fails to provide any teaching or suggestion that they are identical. Applicants submit the abstract of Stackebrandt et al., Reclassification of *Amycolaptosis orientalis* subsp. *lurida* Lechevalier et al. 1986 as *Amycolaptosis lurida* sp. nov., comb. nov., Int. J. Syst. Evol. Microbiol. 54: 267-268 (2004) (copy enclosed)¹ which discloses that even within the species of *A. orientalis*, there are significant differences from other species of the genus in genomic and metabolic properties that it would not have been obvious to one of ordinary skill in the art to make the compounds of the present invention using the claimed microorganisms.

Applicants further submit the abstract of Fiss E. and G.F. Brooks, Use of a siderophore detection medium, ethylene glycol degradation, and beta-galactosidase activity in the early presumptive differentiation of *Nocardia*, *Rhodococcus*, *Streptomyces*, and rapidly growing *Mycobacterium* species, J. Clin. Microbiol. 29(7): 1533-1535 (1991) (copy enclosed), which discloses that *Nocardia* sp. is different from *Rhodococcus* sp. in beta-galactosidase activity and ethylene glycol degradation activity, and that *Nocardia* can be differentiated from *Rhodococcus* by testing these activities. Even if the microorganisms are closely related, as asserted by the Examiner (which Applicants do not submit is the case), it is clear from the Fiss reference that *Rhodococcus* and *Nocardia* are different in their activities. Therefore, even though *Rhodococcus* is able to produce the claimed compounds, it would not have been obvious to one of skill in the art that the claimed compound could be produced by *Nocardia* because *Nocardia* has different

¹ In accordance with M.P.E.P. 609C(3), the documents cited above and below in support of Applicants' remarks are being submitted as evidence directed to an issue raised in the mentioned Official Action, and no additional fee or Certification pursuant to 37 C.F.R. 1.97 and 1.98, or citation on a FORM PTO-1449 is believed to be necessary.

abilities from *Rhodococcus*. Due to the significant differences between microorganisms, it would not have been obvious to one of ordinary skill in the art to make the compounds of the present invention using the claimed microorganisms, in fact, there would have been no motivation to do so.

Similarly, the Davis and Demain documents disclose different species or genera of microorganisms. Davis discloses a genera of microorganisms including *Nocardia* and discloses at most species including *Amycolata autotrophica*, *Streptomyces californicus*, *Amycolatopsis mediterranei*, *Saccharothrix australensis*, *Gilbertella persicaria*, and *Saccharapolyspora erythraea*. Demain discloses a method of converting compactin to pravastatin using a newly isolated strain belonging to the genus *Actinomadura*. Neither Davis nor Demain discloses or provides any guidance to teach or suggest how to make the compounds of the present invention using a claimed microorganism selected from the group of those belonging to the genus *Mycobacterium*, *Corynebacterium*, *Brevibacterium*, *Rhodococcus*, *Gordonia*, *Arthrobacter*, *Micrococcus*, *Cellulomonas* and *Sphingomonas*.

Because of the differences between the microorganisms, it would not have been obvious to one of ordinary skill in the art to make the compounds of the present invention using the claimed microorganisms. Also, as the Examiner herself has established, there are 237 entries for *Nocardia* found on the ATCC database. It would require great experimentation for one of skill in the art to test each of the 237 entries to arrive at the present invention.

At best, this grounds of rejection is based on the impermissible standard that it would be "obvious to try" all of the potential each of the entries to see if the compounds of the compounds of the present invention could be made (which applicants note has not been established). However, a rejection based on the premise that it would be obvious to try a particular compound

or substitution is legally incorrect. Under longstanding case law "obvious to try" is impermissible. In re Tomlinson, 150 U.S.P.Q. 623 (CCPA 1966); Ex parte Argabright et al., 161 U.S.P.Q. 703 (POBA 1967); In re Mercier, 185 U.S.P.Q. 774 (CCPA 1975); In re Goodwin, 198 U.S.P.Q. 1 (CCPA 1978); In re O'Farrell, 7 U.S.P.Q. 2d 1673 (Fed. Cir. 1988). As Judge Rich explained, in distinguishing the facts in O'Farrell from the classic "obvious to try" cases:

...In some cases, what would have been "obvious to try" would have been to vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful...

...In [other cases] what was "obvious to try" was to explore a new technology or general approach that seemed to be a promising field of experimentation, where the prior art gave only general guidance as to the particular form of the claimed invention or how to achieve it...(O'Farrell, at 1681).

In addition, Okazaki merely describes the taxonomical properties of three Actinomycetes belonging to the genus *Nocardia* that is capable of 3 β -hydroxylation, *Nocardia autotrophica* and the two subspecies *N. canberrica* and *N. amethystina*. Okazaki does not disclose, nor is there any guidance in the document to teach or suggest making the compounds of the present invention using a claimed microorganism selected from the group of those belonging to the genus *Mycobacterium*, *Corynebacterium*, *Brevibacterium*, *Rhodococcus*, *Gordonia*, *Arthrobacter*, *Micrococcus*, *Cellulomonas* and *Sphingomonas*.

At most, the combination of these documents would provide hydroxylation of compounds using microorganisms selected from *Amycolatopsis orientalis* ATCC 19795, *Amycolata autotrophica*, *Streptomyces californicus*, *Amycolatopsis mediterranei*, *Saccharothrix*

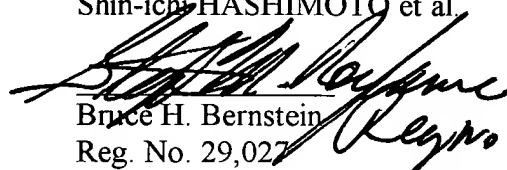
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australensis, *Gilbertella persicaria*, *Saccharopolyspora erythraea*, the genus *Actinomadura*, and the strain *Nocardia autotrophica*.

Accordingly, Applicants respectfully submit that there is nothing in the cited documents, either alone or in combination thereof, that teaches or suggests the claimed invention of using a claimed microorganism selected from the group of those belonging to the genus *Mycobacterium*, *Corynebacterium*, *Brevibacterium*, *Rhodococcus*, *Gordonia*, *Arthrobacter*, *Micrococcus*, *Cellulomonas* and *Sphingomonas*.

In view of the above, Applicants respectfully request the Examiner reconsider and withdraw the foregoing rejections.

Respectfully submitted,
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Reclassification of *Amycolatopsis orientalis* subsp. *lurida* Lechevalier *et al.* 1986 as *Amycolatopsis lurida* sp. nov., comb. nov.

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Amycolatopsis orientalis subsp. *lurida* DSM 43134^T differs significantly from the type strain of *A. orientalis*, *A. orientalis* subsp. *orientalis* DSM 40040^T, and from other species of the genus in genomic and metabolic properties. Its elevation to species status as *Amycolatopsis lurida* sp. nov., comb. nov. is justified.

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Title

Use of a siderophore detection medium, ethylene glycol degradation, and beta-galactosidase activity in the early presumptive differentiation of *Nocardia*, *Rhodococcus*, *Streptomyces*, and rapidly growing *Mycobacterium* species.

Source

Journal of Clinical Microbiology. 29(7):1533-5, 1991 Jul.

Abstract

A simplified scheme for the presumptive early identification of *Nocardia*, *Rhodococcus*, rapidly growing *Mycobacterium*, and *Streptomyces* species is presented. The *Nocardia* and *Streptomyces* spp. and the *Mycobacterium* spp. were positive. The spp. were positive for siderophore activity, but only 25% of the *Rhodococcus* spp. were positive. The *Rhodococcus* and *Mycobacterium* spp. were negative for beta-galactosidase, while the *Nocardia* and *Streptomyces* spp. were positive. The *Nocardia* and *Streptomyces* spp. and the *Mycobacterium* spp. were negative for ethylene glycol degradation, while 75% of the *Rhodococcus* spp. were positive. In combination, these tests were useful for differentiating *Mycobacterium*, *Rhodococcus*, and *Nocardia* species but did not differentiate *Nocardia* from *Streptomyces* species.



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